Care & Guidance Tips Card – Side Effect Management

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IMPORTANT POINTS

- Both boceprevir and telaprevir must be used in combination with peginterferon (PEG IFN) and ribavirin (RBV). PEG IFN and RBV may be dose reduced to manage hematologic side effects, but never discontinued without discontinuing the direct-acting antiviral (DAA).*
- Dose modifications and interruptions are not allowed for either boceprevir or telaprevir. If either is stopped, it cannot be restarted.
- Drug-drug and drug-herb interactions are of significant concern with both boceprevir and telaprevir. Both are substrates and inhibitors of CYP3A4. Coadministration with a drug metabolized by or affected by CYP3A4 may lead to altered drug concentrations, loss of therapeutic activity, or adverse events from drug toxicity. Telaprevir also inhibits P-glycoprotein (P-gp), and boceprevir is a potential inhibitor of P-gp; therefore, co-administration with P-gp substrates may cause similar interactions.
- Both boceprevir and telaprevir may interfere with drug levels of hormonal contraceptives, resulting in ineffective dosing to prevent pregnancies.
- Significant, rapid reduction in red blood cells has occurred with both boceprevir and telaprevir. Monitoring blood counts is required during treatment with both drugs.
- Severe rash requiring dose discontinuation has been reported in 1%–4% of patients on telaprevir. Inform patients to report rashes and monitor until rash resolves.
- Monitor patients with nausea, vomiting, and diarrhea for adequate hydration.
- Provide patients with information on appropriate skin care and hygiene procedures.
- Refer to boceprevir and telaprevir prescribing information for other information.

DRUG – DRUG INTERACTIONS

- Counsel patients on avoiding all herbal products and to contact office before starting any new medication.
- Both boceprevir and telaprevir are substrates and inhibitors of CYP3A4. Telaprevir also inhibits P-gp pathway, and boceprevir is a potential inhibitor based on in vitro studies. Drugs or herbs that are metabolized by these pathways may lead to altered drug concentrations, loss of therapeutic activity, or adverse events from drug toxicities. Refer to prescribing information for other information.
- Hormonal contraceptive agents are not contraindicated, with the exception of drospirenone with boceprevir, but may not be an effective method of birth control during treatment with DAAs.*

Drugs Contraindicated with Boceprevir or Telaprevir[1,2]

Drug Class	Specific Drugs Within Class	Boceprevir	Telaprevir
Alpha 1-adrenoreceptor antagonist	Alfuzosin	X	X
Anticonvulsants	Carbamazepine, phenobarbital, phenytoin	X	–
Antimycobacterials	Rifampin	X	X
Ergot derivatives	Dihydroergotamine, ergonovine, ergotamine, methylergonovine	X	X
Gastrointestinal motility agent	Cisapride	X	X
Herbal products	St. John's wort	X	X
HMG CoA reductase inhibitors	Lovastatin, simvastatin	X	X
Neuroleptic	Pimozide	X	X
Nucleoside reverse transcriptase inhibitor	Didanosine (contraindication for RBV)	X	X
Oral contraceptives	Drospirenone	X	–
PDE5 inhibitor	Sildenafil or tadalafil (when used for the treatment of pulmonary arterial hypertension)	X	X
Sedatives/hypnotics	Midazolam (orally administered), triazolam	X	X

Abbreviations: HMG CoA, 3-hydroxy-3-methylglutaryl-coenzyme A; PDE5, phosphodiesterase type 5; RBV, ribavirin.

* DAA = boceprevir or telaprevir.

1. Victrelis™ [package insert]. Whitehouse Station, NJ: Schering Corporation; 2011.
2. Incivek™ [package insert]. Cambridge, MA: Vertex Pharmaceuticals Incorporated; 2011.

TIPS ON MANAGING SIDE EFFECTS

Cutaneous

- **Allopecia:**

— Avoid coloring/perms/braiding/ponytails; shampoo less.

— Try Selsun Blue® or Nioxin®; scarves/hats; shorter haircut; satin pillowcases; explain that thinning usually resolves after treatment.

- **Injection site reaction pruritus, dry skin, or rash:** Rotate injection sites; antihistamines; topical antipruritics; steroid creams; cool baths; moisturizers; skin lotions; apply cool pack before/after injection.
- **Rash** with telaprevir[§]:

— **Mild or moderate (<50% coverage):** Oral antihistamines, topical steroids, monitor.

— **Severe (≥50% coverage or vesicles/bullae):** As above and stop telaprevir; if not resolved in 7 days, consider stopping RBV and/or PEG IFN.

— **Life threatening (SJS or DRESS with fever, target lesions, mucosal erosions, facial edema, organ involvement):** Stop all anti-HCV treatment, refer for urgent management.

Endocrinologic

- **Thyroid toxicity:** Assess clinical signs/symptoms; check T3 and T4 levels; consider referring to endocrinologist.
- **Diabetes:** Re-educate patient on diet; monitor glucose, HbA1c, consider referring to endocrinologist.

Flulike symptoms

- **Arthralgia, myalgia:** NSAIDs[†], including COX-2 inhibitors, muscle relaxants; low- to no-impact exercise; massage therapy; warm bath/shower; moist heat compresses.
- **Fever:** Acetaminophen[‡] or NSAID[†]; hydration; extremity wraps; electric blanket or hot water bottle for chills.
- **Headache**: Hydration; combination medications used for migraine or cluster headache; acetaminophen[‡] or NSAID[†]; regular times for sleeping and eating; relaxation techniques; exercise.

Gastrointestinal side effects

- **Anorexia:** Determine ideal body weight and caloric needs; snacks, small frequent meals, and supplements; metoclopramide (10 mg PO before meals and qhs); dronabinol (2.5 mg PO BID before lunch, dinner) if no history of substance abuse and not considering liver transplant.
- **Dysgeusia:** Avoid metal utensils or food from cans; change seasonings; oral hygiene.
- **Aphthous ulcers:** Mouthwash containing ES400 50 mL, diphenhydramine 50 mL, dexamethasone 50 mL (swish and spit 4x/d until ulcers clear); antivirals (valacyclovir).
- **Dehydration:** ≥3000 mL fluids/d; avoid caffeine.
- **Diarrhea:** Fiber therapy; OTC antidiarrheals; skin care; sitz baths; monitor hydration.
- **Dyspepsia:** Antacid H_2 blockers; proton pump inhibitors.
- **Nausea, vomiting:** Take RBV with food; antiemetics; avoid cooking smells and foods that trigger nausea; small meals; acupressure bands. Take DAA* with food (20 gm fat snack before telaprevir); avoid greasy, fried, spicy foods; monitor hydration.
- **Anorectal discomfort:** Manage diarrhea; avoid spicy foods; apply anti-inflammatory, lidocaine or barrier creams; skin care; sitz baths.

Hematologic

- **Anemia:** RBV dose reduction as needed (do not totally discontinue if continuing DAA*); check iron/ferritin, vitamin B12 and supplement as needed; consider using growth factors (darbepoetin alfa or epoetin alfa) titrate to target hemoglobin, monitor frequently.
- **Neutropenia:** Low counts may not be a substantial risk in noncirrhotic patients; consider PEG IFN dose reduction (do not discontinue if continuing DAA*); consider G-CSF (300 mcg qw or biw) titrate to desired ANC; monitor frequently.
- **Thrombocytopenia:** Avoid trauma, aspirin-containing products; consider PEG IFN dose reduction (do not discontinue if continuing DAA*); monitor frequently.

Neuropsychiatric

- **Anxiety, irritability:** Exercise; SSRIs; anxiolytics; psychiatric consult; counseling/support programs; avoid caffeine and overstimulating environments; if discontinuing PEG IFN, stop DAA.*
- **Depression:** If pre-existing, stabilize before PEG IFN/RBV; antidepressants; support programs; careful monitoring and support; consider psychiatric consult; PEG IFN dose reduction or discontinuation only if necessary; if discontinuing PEG IFN, stop DAA.*
- **Mania:** Stop antidepressants and seek immediate psychiatric care; consider stopping PEG IFN (stop DAA* if stopping PEG IFN); neuroleptics (olanzapine, risperidone); mood stabilizers (requires psychiatrist); benzodiazepines (clonazepam, lorazepam).
- **Fatigue:** PM administration of PEG IFN; exercise; relaxation techniques; fluids; high-dose venlafaxine; bupropion (75–300 mg/d), methylphenidate (5–20 mg/d), modafinil (100–400 mg/d), duloxetine, buproprion + escitalopram or citalopram; acetaminophen PM.
- **Insomnia:** Administer PEG IFN in AM and RBV second dose before dinner; OTC diphenhydramine; hypnotics; trazodone (25–50 mg/d, use with caution); benzodiazepines; inositol; B vitamins; relaxation techniques; avoid caffeine; drink water early in the day and avoid in the evening.

Ophthalmologic

- **Vision change:** Consider referring to ophthalmologist.

Pulmonary

- **Cough:** Fluids; humidifier; cough drops; guaifenesin ± codeine; hydrocodone syrup.
- **Dyspnea:** Modify activities; avoid smoke, cold air, and allergens; chest x-ray if needed.

*DAA = boceprevir or telaprevir.
[†]Ibuprofen dose should not exceed 2400 mg/d.
[‡]Acetaminophen dose should not exceed 2 g/d.
[§]Courtesy of Cheryl Levine, PhD, FNP. Personal communication. 2011.

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